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TCT-205

High and low platelet reactivity on clopidogrel, prasugrel and ticagrelor in acute coronary syndrome patients: insight from a real-life large cohort

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BACKGROUND Dual antiplatelet therapy with a P2Y12 inhibitor is mandatory in acute coronary syndromes (ACS) undergoing angioplasty. New antiplatelet drugs prasugrel and ticagrelor offer more efficient inhibition compared to clopidogrel. Under P2Y12 inhibitor, platelet reactivity (PR) assessment can predict ischemic and bleeding events. The aim of our study was to compare PR in ACS patients on P2Y12 inhibitors in a real-world setting.

METHODS Platelet reactivity (PR) was prospectively assessed in consecutive patients with recurrent ACS or undergoing high-risk angioplasty. PR was measured 24hrs after last intake of clopidogrel (C) and prasugrel (P), and 12hrs for ticagrelor (T) by flow cytometry measured vasodilatator-stimulated phosphoprotein platelet reactivity index (VASP-PRI) and light transmission agregometry with ADP 20μM (LTA-ADP). High Platelet Reactivity (HPR) was defined as VASP-PRI>50% or LTA-ADP>65% (thresholds previously linked to clinical events). Low Platelet Reactivity (LPR) was defined as VASP-PRI<16% or LTA-ADP<40%.

RESULTS Six hundred and nineteen patients treated with aspirin and C (n=269), P (n=241) or T (n=109) were included from 01/2011 to 07/2013. Mean age was 62±13yrs., 80% were men and 63% had STEMI. Patients on C were older, more often women and admitted for NSTEMI. Inflammatory parameters were lower in this subgroup (C). Clinical and biological characteristics were similar between patients on P and those on T. HPR was more frequent with C compared to P and T and significantly more frequent with P compared to T (Table 1). At the opposite, LPR was significantly more frequent in patients treated with T. In multivariate analysis, the significant predictor of HPR with VASP was P (OR=0.13-CI[0.08-0.22]) or T (OR=0.01-[0.01-0.09]). The significant predictor of LPR with VASP was T (OR=3.37-[2.09-5.44]).

Table 1. Platelet reactivity assessment according to P2Y12 inhibitors and platelet function tests.

	HPR		LPR	
	VASP-PRI	LTA-ADP	VASP-PRI	LTA-ADP
Clopidogrel	48%	37%	7%	14%
Prasugrel	12%*	15%*	27%*	44%*
Ticagrelor	1%*§	2%*§	55%*§	72%*§

*p<0.05 vs clopidogrel; §p<0.05 vs prasugrel.

CONCLUSIONS This observational biological study confirms a more potent platelet inhibition of the new P2Y12 compared to clopidogrel, mainly ticagrelor. The very high rate of LPR found with ticagrelor does not match with the bleeding risk found in the PLATO trial.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy

KEYWORDS Acute coronary syndromes, Platelet aggregation, Platelet function testing

TCT-206

Effect of the α2A-Adrenergic Receptor Genetic Variants on Platelet Reactivity and Adverse Clinical Events in Chinese Patients with Dual Antiplatelet Therapy after Percutaneous Coronary Intervention

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BACKGROUND Platelet α2A-Adrenergic Receptor(ARs) potentiates epinephrine-induced platelet aggregation in response to sympathetic stimulation. Genetic variants of the α2A -ARs are associated with different antiplatelet reactivity. The effect of genetic variants of the α2A -ARs on platelet reactivity and clinical outcomes has not yet been reported in Chinese patients with dual antiplatelet therapy after percutaneous coronary intervention. The aim of this study was to investigate the effect of the α2A -ARs variants on platelet reactivity and clinical outcomes in these patients.

METHODS 1056 patients with dual antiplatelet therapy after percutaneous coronary intervention were enrolled in a single-center registry. All known α2A -ARs genetic variants including rs11195419, rs3750625, rs13306146, rs553668 were detected by the ligase detection reaction and the antiplatelet effect was assessed by thromboelastography. Primary clinical endpoints included cardiovascular death, nonfatal myocardial infarction, target vessel revascularization, and stent thrombosis. The secondary clinical endpoints were angina recurrence, readmission and in-stent restenosis. The follow-up periods were 6 months and 12 months.

RESULTS The frequencies of the α2A -ARs variants were respectively 18.09%, 17.17%, 25.43%, 43.71%. Genotypic distributions of all the variants were in conformity with Hardy-Weinberg equilibrium except rs13306146. Platelet ADP inhibition were significantly different among wild type, heterozygote and homozygote mutated groups carrying rs11195419 genetic variant (53.86±29.78% vs. 50.72±27.80% vs. 39.28±19.53%, P=0.012) or rs3750625 genetic variant (53.71±29.84% vs. 50.93±27.55% vs. 37.524±18.60%, P=0.007) and the homozygote mutated groups have the lowest ADP inhibition of the three groups variants. However, there were no significant differences in ADP inhibition among the rs553668 genotype groups (50.20±27.83% vs. 54.09±29.41% vs. 52.11±30.00%, P=0.158). At the multivariable analysis, the presence of the rs11195419 (95%CI: -0.062- -2.070, P=0.039) or rs3750625 (95%CI: -0.068- -2.281, P=0.023) genetic variants was an independent predictor of the ADP inhibition. However, there were no significant differences in the composite clinical outcome across the rs11195419, rs3750625, rs553668 genotype groups at both 6 and 12 months follow-up period(P>0.05).

CONCLUSIONS The presence of mutated alleles of α2A -AR genetic variants (rs11195419, rs3750625) except rs553668 is associated with decreased ADP-induced platelet reactivity in Chinese patients with DAPT after percutaneous coronary intervention. However, none of the α2A -AR genetic variants significantly influenced the clinical outcomes of DAPT in these patients.

CATEGORIES OTHER: Genomics / Proteomics

TCT-207

Comparative efficacy & safety of Prasugrel, Ticagrelor, standard & high dose Clopidogrel in patients undergoing percutaneous coronary intervention (PCI): A network meta-analysis

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BACKGROUND Higher loading and maintenance dose Clopidogrel overcomes delayed and often variable effect of standard dose Clopidogrel in majority of the patients. However, data comparing this strategy with potent alternatives such as Ticagrelor & Prasugrel are scarce.